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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,700	10/15/2004	Monica Petronella Maria De Maat	101137-56	2836

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EXAMINER	
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ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
09/28/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,700	DE MAAT ET AL.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,14-24 and 41-46* is/are pending in the application.

4a) Of the above claim(s) *10,14-24 and 43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41, 42, 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 10, 14-24, 41-46 are pending. Claims 41, 42, 44-46 are considered on the merits to the extent that they read on the elected species. Claims 10, 14-24, 43 are withdrawn from consideration as being drawn to a non-elected invention.

Applicant's election with traverse of the species, HMW content of at least 80% w/w of the total, in the reply filed on 8/6/09 is acknowledged. The traversal is on the ground(s) that there is no search burden between the species. This is not found persuasive because of the evidence of record, which clearly shows that a reference which anticipates one species does not necessarily anticipate the others. Multiple searches necessary to fully encompass the distinct species and the use of different references for the species provides evidence of burden.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 44-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims recite administering, however, this is a broad term which includes oral, parenteral as well as topical administration. It is not scientifically believable that a patient may be treated for a wound by ingesting a fibrin

matrix or by injection of such a fibrin matrix. Please see suggested claims at the end of the action.

indefinite

Claims 44-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble recites modifying angiogenesis in a patient by administering to the patient a fibrin matrix. However, where the matrix is administered or how is not clear.

Claim Rejections - 35 USC § 102

Claims 41, 42 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Hasegawa *et al.* [U2] or Holm *et al.* [X]

The claims are directed to forming a fibrin matrix from fibrinogen which has a HMW content of at least 80% by weight.

Hasegawa *et al.* disclose fractionating fibrinogen into fractions F1 and F2 with molecular weights of 340 and 325kDa (page 184), forming a fibrin clot (Fig. 2).

Holm *et al.* discloses a method comprising: selecting "normal" fibrinogen, fractionating to form fractions with more or less HMW, LMW and LMW' than the "normal" distribution (Fig 2), forming a fibrin matrix (clot) (page 171).

Claim Rejections - 35 USC § 103

Claims 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/62833 [N] in combination with Holm *et al.* [X] or Hasegawa *et al.* [U2]

The claims are directed to a method comprising: administering to a patient a fibrin matrix made of at least 80% HMW fibrinogen.

Generically, WO 00/62833 discloses a test where a defined matrix of fibrinogen fractions can be clotted and tested for angiogenic potential using endothelial cell ingrowth (page 9, ls. 20-30). Also, a method of promoting angiogenesis in tissue is disclosed.

WO 00/62833 discloses in Example 1, page 29, normal plasma which contains a mixture of fibrinogen types, precipitation by glycine, precipitation by ammonium sulfate 25% saturation which produces a purified fibrinogen with a mixture of types as evidence by fibrinogen bands I and II.

A fraction (Sample 2) of fibrinogen was produced from a mixture of fibrinogen types which had "all its alpha chains intact, but lacked molecules with gamma chains that have an extended carboxy terminal which constitutes approximately 15% of the fibrinogen in plasma".

Another fraction was produced which had all alpha chains intact and contained molecules with both extended and non-extended gamma chains.

Also, Sample 4 contain 20-30% of molecules with degraded alpha chains. Other fractions were also produced with changes in the relative concentration of fibrinogen variants. Sample 4 was clottable.

Holm *et al.* discloses a method comprising: selecting "normal" fibrinogen, fractionating to form fractions with more or less HMW, LMW and LMW' than the "normal" distribution (Fig 2), forming a fibrin matrix (clot) (page 171).

Hasegawa *et al.* disclose fractionating fibrinogen into fractions F1 and F2 with molecular weights of 340 and 325kDa (page 184), forming a fibrin clot (Fig. 2).

The substitution of the fibrin matrices of WO 00/62833 for the fibrin matrices of Holm *et al.* or Hasegawa *et al.* in a method of treating patients with wounds would have been obvious because WO 00/62833 teaches the formation of fibrin matrices with different mixtures of fibrinogen variants and their application for enhancing wound healing. In the absence of evidence to the contrary, one of ordinary skill in the art may substitute any fibrinogen fraction in a fibrin clot for application to a wound. It is noted that the specification does not contain any exemplification of wound treatment in a subject.

One of ordinary skill in the art would have been motivated at the time of invention to produce this composition in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Claims directed to treatment of a patient with HMW and LMW fibrinogen as written below may be allowable upon presentation of evidence of such treatment *in vivo* and the effects thereof. There is no exemplification of wound or burn treatment in a subject in the specification, merely the same *in vitro* type test as in the prior art.

Please carefully consider the following claims, which may be allowable upon presentation of such evidence and a search by the examiner extended to LMW fibrinogen matrix.

47. A method for modifying angiogenesis in a patient comprising topically administering to a wound or burn of the patient, a fibrin matrix made by the process of forming a fibrin matrix from a composition comprising fibrinogen and a pharmaceutically acceptable carrier, wherein the fibrinogen has a high molecular weight content of at least 80% (w/w) of the total fibrinogen amount, forming a fibrin matrix from said

composition, whereby the administration leads to accelerated angiogenesis.

48. A method for modifying angiogenesis in a patient to lessen scar formation or adhesions of a wound comprising topically administering to the wound of the patient, a fibrin matrix made by the process of forming a fibrin matrix from a composition comprising fibrinogen and a pharmaceutically acceptable carrier, wherein the fibrinogen has a low molecular weight content of at least 40% (w/w) of the total fibrinogen amount, forming a fibrin matrix from said composition, whereby the administration leads to a decelerated angiogenesis.

Dependent claims may be added.

The following reference is made of record, Kaijzel *et al.* [U] which appears to be a publication of work done in applicants' lab. Presentation of the *in vivo* evidence in declaratory form is encouraged.

Response to Arguments

Applicants' arguments filed 4/28/09 have been fully considered but they are not fully persuasive. The arguments are answered to the degree that they apply to the new claims and the new rejections.

Applicants argue that there is no disclosure of wound healing in the claims or specification and that something else is intended and is claimed i.e., the modification of angiogenesis. Please note that as a matter of fact, angiogenesis, i.e. new vessel formation occurs during wound healing. It is also known that angiogenesis can occur as part of a disease process, such as diabetic retinopathy. However, there is no possible enablement for a treatment of the angiogenesis in the case of diabetic retinopathy, which is caused by proliferation of blood vessels in the retina. If necessary, a scope of enablement directed at the breadth of the term "modification of angiogenesis" can be instituted. Applicants appear to argue that the references do not teach modification of

angiogenesis. Please note that WO 00/62833 teach a test for angiogenic potential and even test fractions of fibrinogen for such effects. This appears to be essentially the same test as the applicants have performed in the specification.

Conclusion

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). It is applicants' burden to indicate how amendments are supported by the ORIGINAL disclosure. Due to the procedure outlined in MPEP 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 USC 102 or 35 USC 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (571) 272-0922. The examiner can normally be reached on Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, M. Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Sandra Saucier/
Primary Examiner
Art Unit 1651